## Remarks

Applicants thank the Examiner for the helpful interview held on September 23, 2003. Applicants agreed to amend the claims to delete references to cis (Z) isomers, and to resubmit paper #22, the Declaration under 37 C.F.R. § 1.132 of Dr. William Caldwell. The claims have been amended (by canceling claims 21 and 23-25) as agreed and paper #22 has been resubmitted.

## Rejections under 35 U.S.C. § 103 (a)

Claims 21-23, 25-27 and 29 have been rejected under 35 U.S.C. § 103(a) as obvious in view of U.S. Patent 5,861,423 to Caldwell et al. (Caldwell). The rejections are moot with respect to claims 21, 23 and 25. Applicants respectfully traverse these rejections as applied to claims 22, 26, 27 and 29.

As discussed with the Examiner, and as shown in the previously submitted Declaration under 37 C.F.R. § 1.132 by Dr. William Caldwell, compounds with a $CH(CH_3)$ group alpha to the terminal amine show acceptable binding to the relevant receptors, when compared to compounds with a $CH_2$ group alpha to the terminal amine. However, Applicants surprisingly determined that the compounds with the $CH(CH_3)$ group had improved resistance to monoamine oxidase, and therefore, had improved half-lives.

Dr. Caldwell's Declaration (re-submitted as requested by the Examiner) demonstrates the non-obviousness of the claimed compounds. The Examiner had previously reviewed the Declaration and suggested that the Declaration only demonstrated the non-obviousness of trans isomers. With respect to the stereochemistry of the carbon atom identified in the $\underline{C}H(CH_3)$ group with bold and underlining for the Examiner's convenience, the Examiner suggested that the beneficial properties were only shown with respect to a single stereoisomer.

Applicants respectfully disagree with the Examiner's interpretation of the extent of the teachings in Dr. Caldwell's Declaration. With respect to the issue of R and S stereoisomers, as discussed with the Examiner, the Declaration supports the benefits of both stereoisomers. For example, Table 5 of the Declaration shows the beneficial effects of both an R and an S isomer.

Monoamine oxidase inhibition is observed regardless of the stereochemistry at the relevant carbon (alpha to the terminal amine). As this is believed to be a steric effect, there is no sound scientific reason to doubt that this is the case. Accordingly, with respect to the claims as amended, Applicants respectfully request that the Examiner withdraw the rejection.

While Applicants believe that the cis isomers are also useful compounds, to facilitate prosecution, Applicants have cancelled Claims 21 and 23-25, without prejudice, which referred to cis (Z) isomers. The independent claims, Claims 22, 26 and 27, to refer to trans (E) isomers only, and do not include cis (Z) isomers. Applicants reserve the right to pursue claims to the cis (Z) isomers in related applications.

**Provisional Non-statutory Double Patenting Rejections**

Claims 21-27 stand provisionally rejected for non-statutory type double patenting over co-pending U.S. applications 08/631,761 and 09/642,351. The rejections of Claims 21 and 23-25 are moot in view of the cancellation of these claims. With respect to the rejections of pending Claims 22 and 26-29, Applicants previously presented a terminal disclaimer in connection with these applications, which terminal disclaimer has not yet been entered. Applicants respectfully request that the Examiner enter the terminal disclaimer and withdraw the rejections.

## Conclusion

For at least the reasons set forth herein, Applicants submit that pending claims 22 and 26-29 are in condition for allowance. Prompt consideration and action in the form of a Notice of Allowance is thus respectfully requested. Should the Examiner have any questions, he is invited to contact Applicants' undersigned representative at the telephone number below.

Respectfully submitted,

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